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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/084,507	MUNROE ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/28/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Status of Application, Amendments and/or Claims

The amendment filed 17 December 2003 has been entered in full. Claims 1-43 were cancelled. Claims 44-59 are under examination. Applicant's election of Group IV (claims 7, 8, 17 and 18) is acknowledged. Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The information disclosure statement filed 28 February 2002 was received and complies with the provisions of 37 CFR §§1.97 and 1.98. It has been placed in the application file and the information referred to therein has been considered as to the merits.

Objection to Specification

The specification is objected to as not complying with 1.821 (d) of the Sequence Rules and Regulations. When the description or claims of a patent application discusses a sequence listing that is set forth in the "Sequence Listing" in accordance with paragraph (c) of the Sequence Rules and Regulations, references must be made to the sequence by use of the assigned identifier (SEQ ID NO:), in the text of the description or claims of the patent application. For example this occurs on pages 46, line 18; page 47, lines 15-18; page 49, lines 4-5; page 50, lines 10-12 and page 62, lines 7 and 11.

A complete response to this office action includes compliance with this sequence rule compliance. Applicant must submit a response to this Office Action and compliance with sequence rules simultaneously.

The amendment filed 17 December 2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: wherein the response measured in step (c) is selected from *GTPγS binding* (claim 55) and wherein the cytokines are selected from the group consisting of *MCP* (claim 58).

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 55 and 58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

The specification as originally filed does not provide support for the invention as now claimed: "wherein the response measured in step (c) is selected from *GTPγS binding* (claim 55)" and the method according to claim 57, wherein the cytokines are selected from the group consisting of *MCP* (claim 58).

Applicant's amendment, filed 17 December 2003, asserts that no new matter has been added and directs support to Examples 14-19 for the written description for the above-mentioned "limitations". However, the exact wording or connotation of the instant claims is not readily apparent from said sections.

The specification as filed does not provide a written description or set forth the metes and bounds of this "limitations" and does not provide direction for the instant methods encompassing the above-mentioned "limitations" as they are currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as-filed.

Also, see MPEP 2163.05 Changes to the Scope of Claims; it cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office action. Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above or rely upon the limitations set forth in the specification as filed.

Claims 44-51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method of identifying a compound as an agonist for *EDG-2, EDG-3, EDG-4, EDG-5 and EDG-6 receptors* using the readout of NF-κB activation or a method of identifying a compound as an antagonist for *EDG-2, EDG-3, EDG-4, EDG-5 and EDG-6 receptors* using the readout of NF-κB activation and

a method of identifying a compound as an agonist for *EDG-4 receptor* using the readout of IL-8 production or a method of identifying a compound as an antagonist for *EDG-4 receptor* using the readout of IL-8 production

does not reasonably provide enablement for:

a method of identifying a compound as an agonist for an *EDG receptor* or a method of identifying a compound as an antagonist for an *EDG receptor* using the readouts of NF-κB activation and/or IL-8 production. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The subject matter sought to be patented as defined by the claims is not supported by an enabling disclosure because the specification teaches IL-8 production only in the presence of activated EDG-4 receptor (page 35, lines 25-28 and page 37, lines 18-25). In addition, the specification teaches that NF-κB was not induced in the presence of activated EDG-1 receptor (page 45, lines 5-10). Thus the recited assays cannot be used to determine agonist/antagonist activity for all types of EDG receptors.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

Due to the large quantity of experimentation necessary to identify a compound as an agonist or antagonist for all EDG receptors using the recited assays, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims which fail to recite any limitations regarding the types of EDG receptor that can be employed, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 52-59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims are drawn to a method of identifying a compound as an agonist or antagonist of an EDG receptor as identified by the amino acid sequence selected from the group consisting of the amino acid sequence comprising SEQ ID NO:2 and the amino acid sequence comprising SEQ ID NO:4 comprising the steps of: culturing the cells which express an EDG receptor; contacting said culture cells with a

compound to be tested for agonist or antagonist activity at said receptor and measuring an appropriate response indicative of the degree of agonist or antagonist activity.

The instant claims are not supported by an enabling disclosure for the following reasons. SEQ ID NO:2 and SEQ ID NO:4 are polynucleotide sequences, not amino acid sequences. The specification has not taught how to make and/or use amino acid sequences comprising nucleotides sequences.

In addition, the specification fails to teach how to identify a compound as an agonist or antagonist of an EDG receptor wherein the agonist or antagonist activity is measured by modulation of cellular cyclic AMP levels and GTPγS binding. The specification fails to disclose a protocol and the proper parameters/controls when employing these experiments. The specification also fails to teach how to discern the difference between an agonist and antagonist using the recited assays. For example does GTPγS binding indicate antagonist activity? How does an agonist modulate cellular cyclic AMP levels (increase or decrease)?

Due to the large quantity of experimentation necessary to use amino acids comprising nucleotide sequence and the large quantity of experimentation necessary to discern agonist/antagonist activity employing the recited assays, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims which fail to recite any limitations, controls or parameters for the recited assays, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 44-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 44-51 are indefinite because of the recitation, "measuring a response indicative of the degree of NF-κB activation" and "measuring a response indicative of the degree of IL-8 production". The responses are the same for identifying a compound as an agonist and identifying a compound as an antagonists (part c of claims 44, 46, 48, and 50). Thus it is unclear how to discern the difference between an agonist and antagonists. "Indicative of the degree of activation" or "indicative of the degree of production" is vague. The metes and bounds of the instant claims cannot be determined. In addition, it is suggested that the instant claims recite "lysolipid" instead of "LL".

Claims 52-59 are indefinite because of the recitation, "measuring an appropriate response indicative of the degree of agonist or antagonist activity". The claims fail to teach how to discern agonist and/or antagonist activity. For instance, would an antagonist have increased intracellular calcium levels? The metes and bounds of the instant claims cannot be determined.

Claim 52 is indefinite because SEQ ID NO:2 and SEQ ID NO:4 are polynucletides, not amino acid sequences.

Claim 52 is indefinite because of the recitation, "as identified by the amino acid sequence selected from the group consisting of the amino acid sequence comprising SEQ ID NO:2 and the amino acid sequence comprising SEQ ID NO:4". It is unclear if it is the compound or the EDG receptor that comprises SEQ ID NO:2 and SEQ IN NO:4.

Claim 52 is indefinite because it recites two "(a)" and two "(b)"

Claim 55 is indefinite because it is unclear if "modulation of cellular cyclic AMP levels" means increase or decrease.

Claim 55 is indefinite because it recites an improper Markush group.

Claim 57 is indefinite because it is unclear if "determining the level of cytokines production" means increase or decrease relative to a control.

Claim 58 is indefinite because IL-8 and IL-6 are misspelled.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 44-51 are rejected under 35 U.S.C. 102(b) as being anticipated by Hecht et al. (The Journal of Cell Biology, Vol.135/4 November, 1996).

Hecht et al. teach that LPA is the endogenous ligand for EDG-2 receptor (page 1075, 5th-6th paragraph and Discussion, page 1078-1080). Hecht et al. teach that other phospholipids did not produce the same effect as LPA (sustained cell rounding)(page 1075 and Table III). The cell were grown in low serum medium (page 1073, material and methods, cell culture). The instant claims are drawn to methods of identifying

compounds as an agonist or antagonists for an EDG receptor comprising measuring a response indicative of the degree of NF-κB activation and indicative of the degree of IL-8 production. The instant claims do not have a precise step of actually measuring NF-κB activation or measuring IL-8 production. Thus inherently any activation of the receptor would ultimately be measuring something that is *indicative of NF-κB activation and/or indicative of the degree of IL-8 production*. It is suggested that Applicants amend to claims to recite measuring NF-κB activation or measuring IL-8 production.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RMD
2/18/04

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